

Translation

PATENT COOPERATION TREATY

PCT/JP2003/015315



PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference FP0194PCT	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2003/015315	International filing date (<i>day/month/year</i>) 01 December 2003 (01.12.2003)	Priority date (<i>day/month/year</i>) 03 December 2002 (03.12.2002)
International Patent Classification (IPC) or national classification and IPC A61K 31/437, A61P 25/14, 25/16, 25/28, 43/00, C07D 471/04		
Applicant KYORIN PHARMACEUTICAL CO., LTD.		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of _____ sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>	
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>	

Date of submission of the demand 04 March 2004 (04.03.2004)	Date of completion of this report 02 December 2004 (02.12.2004)
Name and mailing address of the IPEA/JP	Authorized officer
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2003/015315

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ The international application as originally filed/furnished
- ☐ the description:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the claims:
- pages _____, as originally filed/furnished
- pages* _____, as amended (together with any statement) under Article 19
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the drawings:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP03/15315

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-4, 6	YES
	Claims	5	NO
Inventive step (IS)	Claims	1-4, 6	YES
	Claims	5	NO
Industrial applicability (IA)	Claims	1-6	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: JP, 11-302190, A (Michihiro Fujiwara, et al.), 2 November, 1999 (02.11.99)

The above document describes that Ibudilast is used for improvement of dementia such as cerebral vascular dementia and Alzheimer's dementia (paragraph [0002]).

Document 2: WO, 01-40226, A1 (Toray Industries, Inc.), 7 June, 2001 (07.06.01)

The above document mentions Ibudilast as an example of a preventive/curing drug for cerebral angiopathy and suggests that it is used for prevention and treatment of diseases with dementia (specification, page 61, line 16 to page 62, line 5).

Document 3: Drug for Improvement of Brain Circulation and Metabolism, and How to Use It, (Hirotohi Kasahara, et al.), Clinica, 1990, 17 (5), pages 256-262

The above document describes that cerebral circulation improvement drugs are widely used for treatment of dementia diseases of old age.

Claim 5

The subject matter of claim 5 does not appear to be novel or to involve an inventive step in view of documents 1-3 cited in the ISR.

Document 1 shows that Ibudilast, which has a structure that is encompassed by the general formula (1) of the claim of the present international application, is known as a drug for improvement of cerebral circulation, and is also used for improvement of dementia of Alzheimer's disease. It is not considered that the case of using Ibudilast for treatment of dementia caused by Alzheimer's disease, described in document 1, and the case of using Ibudilast for treatment of Alzheimer's disease in the invention of the present application, are substantially different from each other. In addition, Ibudilast is used for improvement of various signs of dementia such as cerebral vascular dementia (documents 1-3), and it is well known that dementia is one of the typical symptoms of Alzheimer's disease that develops in old age, and so it is not considered that the case of using Ibudilast for treatment of dementia diseases in old age, described in documents 1-3, and the case of using Ibudilast for treatment of dementia caused by Alzheimer's disease in the invention of the present application, are substantially different from each other.

Claims 1-4 and 6

The subject matters of claims 1-4 and 6 appear to involve an inventive step in view of documents 1-3 cited in the ISR.

Documents 1-3 do not describe or suggest that the compounds represented by the general formula (1) of the claims of the present application are phosphodiesterase 10A inhibitors, or that such compounds can be used as treatment/preventive drugs for Parkinson's disease, for Huntington chorea, and for schizophrenia. Documents 1 and 2 describe that Ibudilast, a compound encompassed in those represented by the formula (1) of the present application, has an effect of improving cerebral bloodstream; however, the relationship of that effect with Parkinson's disease, Huntington chorea, or schizophrenia is unclear from those documents.